

AMENDMENTS

Please enter the following amendments:

Amendments to the claims:

This listing of claims will replace all prior versions, and listings, of claims in the application:

1. **(previously presented)** A synthetic oligonucleotide comprising a nucleotide sequence consisting of 21 nucleotides of the sequence set forth as SEQ ID NO: 5, the nucleotides being linked via phosphorothioate internucleotide linkages, and the oligonucleotide being specifically complementary to nucleotides ^{9 to 30 of SEQ ID No. 8, which comprises} ~~324 to 345~~ of a conserved *gag* region of the HIV-1 genome, wherein the synthetic oligonucleotide does not have the sequence set forth as SEQ ID NO: 4 ~~and is not complementary to the conserved gag region of the HIV-1 genome beyond nucleotides 324 to 345.~~
2. **(original)** The oligonucleotide of claim 1, wherein the nucleotides comprise at least two 3'-terminal ribonucleotides, at least two 5'-terminal ribonucleotides, or at least two 3'-terminal and at least two 5' terminal ribonucleotides.
3. **(original)** The oligonucleotide of claim 2, wherein the ribonucleotides are 2'-substituted ribonucleotides.
4. **(original)** The oligonucleotide of claim 3, where the 3'-substituted ribonucleotides are 2'-O-alkyl ribonucleotides.
5. **(original)** The oligonucleotide of claim 4, wherein the ribonucleotides are 2'-O-methyl ribonucleotides.
6. **(previously presented)** The oligonucleotide of claim 2, wherein the nucleotides consist essentially of four 3'-terminal ribonucleotides and four 5'-terminal ribonucleotides, flanking 13 deoxynucleotides.

7. **(original)** The oligonucleotide of claim 6, wherein the ribonucleotides are 2'-O-methyl ribonucleotides.

8. **(original)** The oligonucleotide of claim 1, having SEQ ID NO:1.

9. **(original)** The oligonucleotide of claim 1, having SEQ ID NO:3.

10. **(original)** The oligonucleotide of claim 7, having SEQ ID NO:1.

11. **(original)** The oligonucleotide of claim 7, having SEQ ID NO:3.

12. **(original)** The oligonucleotide of claim 1, having SEQ ID NO:2.

13. **(canceled)**

¹³ ~~14.~~ **(original)** The oligonucleotide of claim 1, which inhibits HIV-1 or HIV-2 infection in a cell.

¹⁴ ~~15.~~ **(original)** The oligonucleotide of claim 1, which exhibits antiviral activity against HIV-1 and HIV-2.

16. **(canceled)**

17. **(canceled)**

18. **(canceled)**

19. **(canceled)**

20. (canceled)

21. (canceled)

22. (canceled)

23. (canceled)

24. (canceled)

25. (canceled)

26. (canceled)

27. (canceled)

28. (canceled)

29. (canceled)

15. ~~30.~~ (currently amended) ~~The method of claim 16, wherein the oligonucleotide is administered~~
A method of treating HIV-1 or HIV-2 infection in a human comprising
administering intravenously to the human a synthetic oligonucleotide in an amount
effective to inhibit the proliferation of HIV-1 or HIV-2, the oligonucleotide comprising a
nucleotide sequence consisting of 21 nucleotides of the sequence set forth as SEQ ID NO: 5, the
nucleotides being linked via phosphorothioate internucleotide linkages, and the oligonucleotide
being specifically complementary to nucleotides 324 to 345 of a conserved gag region of the
HIV-1 genome. ^{9 To 30 of SEQ ID NO. 8, which comprises}

16. ~~31.~~ (original) A pharmaceutical formulation comprising the oligonucleotide of claim 1 in a pharmaceutically acceptable carrier.

17. ~~32.~~ (original) A pharmaceutical formulation comprising the oligonucleotide of claim 6 in a pharmaceutically acceptable carrier.

18. ~~33.~~ (original) A pharmaceutical formulation comprising the oligonucleotide of claim 7 in a pharmaceutically acceptable carrier.

34. (canceled)

35. (canceled)

36. (canceled)

37. (canceled)

38. (canceled)

19. ~~39.~~ (currently amended) A method for introducing an intact oligonucleotide into a mammal, the method comprising the step of orally administering to the mammal ~~the oligonucleotide of claim 7~~ a synthetic oligonucleotide comprising a nucleotide sequence consisting of 21 nucleotides of the sequence set forth as SEQ ID NO: 5, the nucleotides being linked via phosphorothioate internucleotide linkages, wherein the nucleotides consist essentially of four 3'-terminal 2'-O-methyl ribonucleotides and four 5'-terminal 2'-O-methyl ribonucleotides, flanking 13 deoxynucleotides and the oligonucleotide being specifically complementary to nucleotides 324-345 of a conserved gag region of the HIV-1 genome, wherein the synthetic oligonucleotide does not have the sequence set forth as SEQ ID NO: 4 and is not complementary to the conserved gag region of the HIV-1 genome beyond nucleotides 324 to 345,

whereby the oligonucleotide is present in intact form in the systemic plasma following oral administration.

40. (canceled)

41. (canceled)

et al., eds.) Cold Spring Harbor Laboratory, Cold Spring Harbor, NY, pp. 235). The oligonucleotides of the invention have been designed to bind to this region of RNA and DNA, thereby disrupting its natural stability and resulting ultimately in the inhibition of viral packaging and translation of *gag* mRNA. The specific sequence to which the oligonucleotides of the invention are complementary is nucleotides 324-345 of the *gag* region of HIV-1. This sequence is very conserved among strains of HIV-1, as shown below in TABLE 1.

TABLE 1

15	Sequence of:			
	324-345→	TCTTCCTCTCTACCCACGCT		
	CONSENSUS	CGGAGGCTAGAAGGAGAGAGATGGGTGCGAGAGCGTCAGTA	(Seq #1 No. 8)	
20	Strains of HIV-1			
	HTLV/LLAV	G		A
	HIVLAI	G		A
	HIVNL43	G		G
	HIVMN	G		G
25	HIVJH3	G		A
	HIVOI	G		A
	HIVCDC4	G		A
	HIVRF	G		A
30	HIVMAL	G		A
			(African)	
	HIVU455	A		A CCTCAG
				(Ugandan)
35	HIVSF2	(GA)	4G	G
	HIVNDK		G	A